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Declaration

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Dedication

I would like to dedicate this MMED to my deceased mother, Vukani Mandlovu Matshikiza and to Professor Alan Bryer, who supported me throughout this project. Thank you for always motivating and encouraging me. Your constant motivation “just do it” reminded me that it can be done.

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It has been a privilege working under the supervision of Professor Alan Bryer. He was instrumental in completing this task through constant support and guidance. I would like to thank Professor Badri Motassim who made the statistical aspects so simple to understand and for his support in statistics and extraction of the data.

Acronyms and abbreviations

BAO = Basilar artery occlusion

CT = Computed tomography

DNT = Door to needle time

EMS = Emergency medical service

EVT = Endovascular thrombectomy

FAST = Face-Arm-Speech-Time

GSH = Groote Schuur Hospital

HSFSA = Heart and Stroke foundation of South Africa

HREC = Human Research and Ethics Committee

IVT = Intravenous thrombolysis

NNT = Number needed to treat

MR = Magnetic resonance

RCT = Randomized controlled trial

SA = South Africa

Definitions of terms

Door-to-needle time = time interval from arrival at emergency department (ED) to the administration of intravenous thrombolysis

Door-to-CT brain time = time interval from arrival at ED to CT brain.

Symptom-to-door time = time interval from symptom onset to arrival at ED.

Symptom-to-needle time = time interval from symptom onset to the administration of thrombolysis

ABSTRACT

Title

Barriers to acute stroke care at a tertiary Hospital in the Western Cape.

Background

Stroke guidelines recommend treatment of acute stroke as a medical emergency. In many countries prolonged delays occur before patients with acute stroke receive medical attention. Only a small percentage of patients are assessed in hospital within the time window for reperfusion therapy. There is limited available published data concerning barriers to acute stroke care in South African patients. The aim of this study was to determine the pre-hospital barriers and in-hospital delays to emergency care for patients presenting to Groote Schuur Hospital (GSH) with acute stroke.

Methods

Eligible patients included were those with a clinical and radiological diagnosis of acute stroke who presented to GSH Emergency Unit and required admission for more than 24 hours. The study was a prospective, observational study with two components: a semi structured interviewer administered questionnaire and a record review of ischaemic stroke patients' clinical notes within 48 hours of admission to GSH. GSH is a tertiary/academic level hospital in Cape Town, Western Cape province, South Africa. Recruitment took place over a 6-week period.

Results

Demographics: 50 patients were included, with a median age of 61,5 (IQR 44,7 – 70,2) years; gender: females, 29 (58%). **Ethnicity:** Mixed African ancestry 38 (76%), Black 11 (22%).

Pre- hospital barriers: The median distance to hospital was 12,7 (IQR 10,2 – 17,6) km. Most patients 32 (64%) called for assistance immediately. Frequent reasons cited for delays: waiting for improvement, 7 (38,9%) and failure of symptom recognition 4 (22%). Most patients used their own private transport, 32 (64%) and half of the patients (25) presented directly to GSH.

In- hospital delays: The median time interval from arrival at the Emergency Unit to doctor assessment for all the patients was 67,5 (IQR 19,75 – 128,5) minutes. The median door to CT brain time interval for all patients was 5,1 (IQR 1,7 – 10,2) hours and 3,1 (IQR 0,8 – 9,6) hours for those patients that arrived within the thrombolysis time window. Only 21 of 50

patients were referred and assessed by the stroke unit team. Only 3 of the 21 patients received intravenous thrombolysis and none received mechanical thrombectomy.

Conclusion:

There majority of the patients who arrived at GSH early after symptom onset used their own private transport and lived close to hospital. Pre-hospital barriers were failure to recognize symptoms, patients hoping for clinical improvement, delays in ambulance transport and routing via secondary hospitals. In hospital delays were prolonged door to doctor assessment and door to CT Brain time intervals.

INTRODUCTION

Acute ischemic stroke should be treated as a medical emergency and evaluated with minimum delay, regardless of severity of deficits. Time loss due to pre-hospital and in-hospital delays remains a problem especially for patients that are potential candidates for reperfusion therapy including intravenous thrombolysis and or endovascular therapy (EVT). Reperfusion therapy is more effective when given early after symptom onset. Brain tissue is very sensitive to ischemia, and neurons begin to die shortly after oxygen deprivation. The benefit of reperfusion therapy is strongly time dependent and all efforts should be made to initiate reperfusion therapy as soon as possible. Many patients that could potentially benefit from this type of treatment are precluded due to prolonged pre-hospital and in-hospital delays.

There has been limited progress in management of stroke patients in developing countries and data on stroke care in these countries is sparse. Stroke guidelines are continuously developed and updated in the high-income countries but their applicability for use in developing regions is questionable. The number of stroke patients receiving hyper-acute stroke care including the option of intravenous thrombolysis in developing countries is very low. The objective of this study is an assessment of pre-hospital and in-hospital barriers and limitations to hyper-acute stroke care at a tertiary hospital in the Western Cape of South Africa.

The study methodology is a prospective, observational evaluation of 50 ischaemic stroke patients admitted to Groote Schuur Hospital (GSH) Emergency Unit (EU) over a period of six weeks. Most of the patients admitted to our hospital are either Black or of mixed African ancestry from lower income groups, many living in informal settlements. Pre-hospital barriers to early treatment that were assessed included failure of symptom recognition, delay in calling for help, emergency medical service (EMS) response, distance to the hospital and delays due to routing via community health centers (CHC) and secondary hospitals without availability of reperfusion therapy for suitable patients with acute ischemic stroke.

The in- hospital delays that were evaluated included the efficiency of the triage process for stroke patients and delays in obtaining the required mandatory investigations such as CT brain scan that could potentially result in suitable patients being precluded from receiving reperfusion therapy within the acceptable time window after symptom onset.

By identifying the causes of pre and in-hospital delays to acute stroke care, data from this study will be used to address and improve existing pathways to overcome these barriers. If these delays can be significantly reduced, this should impact positively on hyper-acute stroke care in our hospital potentially leading to improved outcomes for our stroke patients.

PART A : Structured Literature Review

1. Epidemiology of stroke

Stroke is a clinical syndrome with rapid onset of focal neurological symptoms due to no other apparent reason but a vascular one, leading to permanent brain tissue damage (Albers et al., 2002). Stroke is the second-leading cause of death worldwide after ischemic heart disease (Lozano et al., 2012). In 2010, stroke was responsible for 5.3 million deaths or 1 in 10 deaths worldwide and the absolute number of people affected by stroke has been increasing yearly since 1990, along with the numbers of disabled stroke survivors and deaths related to stroke (Krishnamurthi et al., 2013). More than 80% of stroke burden occurs in low and middle-income countries (LMICs), yet reliable data on stroke epidemiology, particularly incidence and morbidity is scarce in these settings (Sajjad et al., 2013). In South Africa (SA), stroke is responsible for some 25,000 deaths annually and 95,000 people lived with disability, yet few published studies report on the epidemiology of stroke in rural parts of the country. We do not know the incidence of stroke in South Africa, but we do have some data on stroke mortality and prevalence that highlight the impact of stroke on the population (Connor et al., 2007).

2. Time is brain concept

The phrase “time is brain” emphasizes that human nervous tissue is rapidly and irretrievably lost as stroke progresses and that any therapeutic interventions should be emergently pursued (Gomez et al., 1993). Recent advances in stroke neuroimaging permit an estimate calculation of the quanta of brain tissue that is lost per unit time in acute ischemic stroke. The average duration of non-lacunar stroke evolution is 10 hours (range 6 to 18 hours), and the average number of neurons in the human forebrain is 22 billion. In patients experiencing a typical large vessel acute ischemic stroke, it is estimated that 120 million neurons, 830 billion synapses, and 714 km (447 miles) of myelinated fibers are lost each hour. In each minute, 1.9 million neurons, 14 billion synapses, and 12 km (7.5 miles) of myelinated fibers are destroyed. Quantitative estimates of the pace of neural circuitry loss in human ischemic stroke emphasize the time urgency of stroke care (Saver et al., 2006). A recent study attempted to estimate the potential beneficial effect over a patient’s lifetime of rapid initiation of stroke thrombolysis in suitable patients with acute ischemic stroke. The authors estimated that each minute of time saved from symptom onset-to-treatment conferred on average 1.8 days of extra healthy life and each 15-minute decrease in treatment delay could provide an average equivalent of 1 month of additional disability-free life (Meretoja et al., 2014).

3. Stroke management

Recognition of stroke symptoms by the patient at risk, family members, the general public, and health workers is an important factor that determines a prompt response and initiation of management. Given the narrow time window for reperfusion therapy, patients with symptoms should seek urgent medical attention. Paramedics should be able to recognize symptoms and signs of stroke and diagnose stroke using simple instruments such as the Face-Arm-Speech-Time test, FAST (Nor et al., 2004). If it is feasible to transport a stroke patient to a hospital with the appropriate resources, expertise, and protocols in place for reperfusion therapy within the recommended time interval for such treatment, then the patient should be transferred directly to such a stroke centre. Ideally EMS personnel should be able to provide pre-hospital notification to the receiving hospital that a suspected stroke patient is on route so that the appropriate hospital resources may be mobilized before patient arrival. The key to reducing in-hospital delays is to do as little as possible after the patient has arrived at the emergency room and as much as possible before that, while the patient is being transported (Meretoja et al., 2012). In the emergency unit, stroke patients should be promptly identified, stabilised and evaluated urgently including receiving an urgent CT brain scan. Eligible patients for reperfusion therapy within the time window for treatment (with no contra-indications) should be promptly informed of both the potential benefits and the risks of this type of treatment so that a decision can be made whether to proceed with such treatment as the potential benefits for both intravenous thrombolysis and endovascular therapy is time-dependent (“time” is quite literally “brain” and the sooner the treatment is given after symptom onset, the greater the chance of a successful outcome).

3.1 Prehospital management of stroke

According to the most recent American Stroke Association guidelines, protocols should be used to guide pre-hospital stroke care (Powers et al., 2018). These concerns maintaining physiological homeostasis and management of early complications or co-morbidities of stroke, such as impaired consciousness, seizures and vomiting or hemodynamic instability. General measures by an attending physician or paramedic include assessment of breathing and maintaining the airway (providing oxygen if necessary, to maintain saturation over 95%), managing hemodynamic instability, and maintaining hydration (patients should receive nil by mouth until swallowing has been assessed to prevent aspiration). Blood glucose should be measured, and hypoglycemia should be promptly treated if present. The information

concerning the history of event, including time of onset, signs and symptoms, and previous medical, drug and social history should be obtained from patient and/or informant. All medication should be brought to hospital with the patient and the informant should be encouraged to accompany the patient.

3.2 Emergency medical service (EMS)

Emergency medical service (EMS) refers to the full scope of pre-hospital stroke care, ambulance activation and dispatch, emergency medical response, triage and stabilization in the field, ground or air ambulance transport. The EMS threshold of stroke suspicion should be set low, to be sensitive rather than specific, as the final diagnosis will be made at the admitting hospital and an initially delayed diagnosis can prevent a patient from receiving effective therapy (Meretoja et al., 2012). EMS personnel should obtain information from the patient, family members, or other witnesses about the suspected stroke event (presenting symptoms, time of onset or time of symptom recognition or time last known well, and sequence of events) as well as information concerning comorbid conditions, current medications, and any formal or informal advance directives that may influence care by EMS and in the emergency department (ED). EMS personnel should provide pre-hospital notification to the receiving hospital that a suspected stroke patient is en route so that the appropriate hospital resources may be mobilized before patient arrival. (Bryer et al., 2010) Pre-notification to the admitting hospital with a stroke service by the EMS has been shown to reduce in-hospital delays, improve intravenous thrombolysis rates, reduce lengths of hospital stays and mortality, and is recommended both in the American and European stroke guidelines (Adams et al., 2007). Each potential stroke patient should be evaluated as an emergency similar to myocardial infarction or trauma and ambulances should be dispatched with high priority (Casaubon et al., 2015).

3.3. Radiology

Ideally, every patient with stroke should have a brain imaging study (CT brain or MRI brain scan) to confirm the stroke and exclude stroke mimics although this is not feasible in all South African hospitals because of logistic and resource constraints. Non-contrast CT brain scan is the most cost-effective strategy for imaging acute stroke patients (Wardlaw et al., 2004). At our center we have a CT scan available on site 24 hours a day and a dedicated stroke response service and can offer reperfusion therapy including both intravenous thrombolysis and endovascular therapy for appropriate patients with ischemic stroke who arrive within therapeutic window. Urgent brain imaging is required and mandatory to rule out brain

haemorrhage as this cannot reliably be predicted clinically and is an absolute contra-indication to reperfusion therapy.

Some centers prefer to use MRI scan as first-line routine investigation for acute stroke, but CT scan is more readily accessible and available at most stroke centres and has the advantage of a quicker scanning time. Diffusion-weighted MRI (DWI) is more sensitive than CT brain for detection of early ischemic changes. (Ay et al., 2002).

With the advent of endovascular therapy (mechanical thrombectomy) being available at our centre, vascular imaging with CT angiography is used to identify the site of a proximal arterial obstruction suitable for an intra-arterial intervention. Advanced CT or MRI imaging (such as perfusion diffusion mismatch) has been shown to be of value in selecting patients for reperfusion beyond the current time intervals but is not widely available in SA. (Nogueira et al., 2018). Whichever radiologic modality is used to select patients, time to initiate reperfusion therapy remains of the essence with better outcomes associated with earlier intervention following onset of stroke symptoms. This further emphasizes the need for rapid assessment and treatment of acute ischemic stroke (AIS).

4. Reperfusion therapy

Rapid, safe and effective arterial recanalization to restore blood flow and improve functional outcome remains an objective of hyper-acute ischemic stroke management (Bryer et al., 2010). Successful recanalization has the potential to ameliorate many complications and the need for rehabilitation, but is attempted in only few ischemic stroke patients, mostly due to failure of the patient and the healthcare system to respond rapidly enough (Meretoja et al., 2012). Prevention is the key to reduce the burden of stroke but once it fails, reperfusion therapy in selected patients is the only acute medical treatment shown to reduce the brain damage and improve patient outcomes (Ringleb et al., 2008). Ideally patients with disabling acute ischemic stroke should be screened without delay by a physician with stroke expertise to determine eligibility for both medical treatment with intravenous recombinant tissue plasminogen activator (IV r-tPA) within 4.5 h from stroke symptom onset and or endovascular therapy (EVT) within a six-hour window from stroke symptom onset for ischemic stroke patients with proven proximal large artery occlusions (Casaubon et al., 2015) . All eligible patients should receive reperfusion therapy as soon as possible after hospital arrival, with a target door-to-needle time of less than 60 minutes. Treatment should be initiated as soon as possible after

patient arrival following brain imaging. Every effort should be made to ensure door-to-needle times are routinely monitored and improved.

This narrow window of opportunity and low levels of awareness about stroke and inefficient public transport systems represent the largest obstacle to more widespread use of reperfusion treatment. These and other issues, such as cost, expertise, and the availability of required resources necessary to administer this type of treatment, have caused concerns that intravenous thrombolysis may not be a viable option for treating stroke in many developing countries (Wasserman et al., 2012).

4.1 Intravenous thrombolysis

Intravenous thrombolytic therapy with recombinant tissue plasminogen activator (IV r-tPA) is an accepted therapy for acute ischemic stroke within 4.5 hours of onset (Bluhmki et al., 2009). Intravenous thrombolysis should be administered at a hospital with rapid triage of stroke patients, established protocols for use of IV r-tPA, where there is strict adherence to inclusion and exclusion criteria, and where good post-treatment care is available. Thrombolytic therapy should only be given if the diagnosis is established by a physician with expertise in the diagnosis of stroke and who is aware of the risks of this treatment. Imaging of the brain (CT scan or MRI) must be done prior to treatment with IV r-tPA and assessed by physicians with expertise in reading and interpreting the imaging study and when hemorrhage is excluded.

The landmark National Institute of Neurological Disorders and Stroke (NINDS) rt-PA trial in the USA in 1995 demonstrated that patients receiving this intervention were 30% more likely to survive with minimal disability resulting in a 12% absolute increase in the proportion having excellent functional outcomes at 3 months. IV r-tPA at a standard dose given within 4.5 hours after ischemic stroke onset, significantly improves clinical outcome, compared with placebo (Hacke et al., 2008). Treatment benefit is time-dependent, and the number needed to treat (NNT) to get one more favorable outcome drops from 4 during the first 90 minutes through to 7 at 3 hours, and towards 14 between 3 and 4.5 hours. The sooner the treatment is given, the greater the chance of a successful outcome. (Hacke et al., 2008). A recent meta-analysis has shown that irrespective of age or stroke severity, and despite an increased risk of fatal intracranial haemorrhage during the first few days after treatment, intravenous thrombolysis significantly improves the overall odds of a good stroke outcome when delivered within 4.5 h of stroke onset, with earlier treatment associated with bigger proportional benefits. (Embersson et al., 2014). Meretoja and others demonstrated that minutes saved in stroke thrombolysis

translate to days, weeks, and months of disability-free life over a patient's lifetime. Therefore, all attempts should be made to reduce treatment delays (Meretoja et al., 2014).

4.2 Endovascular therapy

Until recently, the only licensed treatment for acute ischemic stroke was intravenous thrombolysis with recombinant tissue-plasminogen activator (IV r-tPA). The net benefit of IV r-tPA for patients with severe stroke due to large proximal artery occlusion is reduced compared to more distal occlusions. Early recanalization generally occurs in less than 30% of patients with internal carotid, proximal middle cerebral artery or basilar artery occlusions (Bhatia et al., 2010) with good clinical outcome occurring in less than 25% of patients with proximal occlusions when treated with IV r-tPA alone (Fischer et al., 2005). Important independent risk factors predicting poor outcome post intravenous thrombolysis are the length and location of the arterial thrombus. (Hirano et al., 2010) The reduced efficacy of intravenous thrombolysis in the treatment of proximal occlusions with a larger clot burden treatment led to efforts to remove larger arterial clots using mechanical means.

The recent publication of several clinical trials evaluating the effect of mechanical thrombectomy in patients with ischemic strokes due to proximal occlusions in the anterior circulation have demonstrated that the procedure can accelerate the process of recanalization, increase the recanalization rate and improve outcomes in such patients. These findings have revolutionized the care of patients with acute ischemic stroke due to large vessel occlusion in comprehensive stroke centres where interventional procedures such as mechanical thrombectomy can be performed. These RCTs showed that endovascular therapy (EVT) had a clinical benefit when it was performed within 6 hours after the onset of stroke symptoms (Berkhemer et al., 2015). Data from recent clinical trials indicate that the use of intravenous thrombolysis with r-tPA within 4,5 hours combined with EVT within 6 hours is superior to IV r-tPA alone (Campbell et al., 2015) for proximal occlusions amenable to endovascular therapy as demonstrated by CT or MR angiography. The efficacy of this treatment in suitable patients surpasses any previous therapy in stroke medicine, with a number needed to treat of less than 3 for improved functional outcome. EVT has recently become available at GSH by year 2016 as part of the stroke service and is a collaborative effort between the stroke unit, neurosurgery, and radiology. However, only a very small minority of stroke patients in South Africa are likely to qualify for EVT at present, given the availability of the required expertise, time constraints

for treatment, resource limitations, lack of comprehensive stroke units, all of which are barriers to hyper-acute stroke care.(Bryer et al., 2010).

5. Acute stroke care in developing countries

Despite robust evidence of efficacy of reperfusion therapy for suitable patients with acute ischemic stroke we have encountered relatively few patients that present to GSH Emergency Unit early enough after symptom onset to potentially benefit from revascularization therapies such as intravenous thrombolysis and or endovascular therapy, and to receive appropriate treatment to maintain physiologic homeostasis and prevent early complications. Bryer and Wasserman assessed the short-term outcomes and safety of intravenous r-tPA for the treatment of stroke at Groote Schuur Hospital and only identified 42 patients in 11 years (Bryer et al., 2012). As with many other low and middle-income countries, most patients in our setting experience prolonged delays between symptom onset and access to acute stroke care. Consequently, only a small proportion of stroke patients admitted to our hospital are potentially suitable candidates for revascularization therapy. If specific barriers to emergency care of stroke patients are identified and addressed, more patients could benefit from this type of treatment in conjunction with standard treatment with measures directed at maintaining physiological homeostasis and preventing early complications could be implemented earlier.

Khalema and colleagues (2018) undertook a retrospective record review of all patients who presented with clinical features of stroke to a tertiary academic emergency department (ED) in Johannesburg, South Africa, from 01 January to 31 December 2014. Their aim was to investigate the time from stroke symptom onset to presentation to the ED, the time from arrival to CT scan acquisition and the potential influencing factors. Patients presenting with stroke were identified through the ED triage and patient registers, as well as the radiology department CT reports. They included 232 eligible stroke patients. The median time to presentation to the ED was 33 hours with the majority of patients (81.3%) presenting after the 4.5 hours window for thrombolysis. The median time to CT was 8 hours. Only 3.9% of patients had a CT scan within one hour of arrival and none of the patients were thrombolysed. They concluded that, the majority of patients presented late to hospital. Their presentation time to ED almost parallels other low- and middle-income countries like Nigeria and China but is lower than in developed countries like England (<3 h presentation rate of 39.5%) and Australia (31.3% presenting within 4.5 h). Additionally, the majority of their patient population had a CT scan performed after 1 hour from ED arrival – this is longer than the

25-minute recommendation by the American Heart Association.

Wasserman and colleagues (2009) assessed discharge planning of stroke patients, available resources and continuity of care between hospital and community in a remote rural setting in South Africa. They sought to determine outcomes, family participation and support needs, and implementation of secondary prevention strategies. A trained field worker using a structured questionnaire assessed thirty consecutive stroke patients from the local hospital clinically at time of discharge and re-assessed 3 months after discharge in their homes. All patients were discharged into family care as there was no stroke rehabilitation facility available to the community. Of the 30 patients recruited, 20 (66.7%) were alive at 3 months, 9 (30%) had died, and 1 was lost to follow-up. The 3-month mortality rate was high. Most survivors improved functionally but were left with significant disability. The authors recommended measures to improve family education and the level of home-based care to reduce the degree of functional disability in rural stroke patients.

Pandian and colleagues (2017) performed a systematic review on strategies to improve stroke care services in low- and middle-income countries (LMICs). They were attempting to determine the quality of existing stroke-care services in LMICs and to highlight indigenous, inexpensive, evidence-based implementable strategies being used in stroke-care. They concluded that some strategies are economic, feasible and reproducible but remain untested and that data on their outcomes and sustainability is limited.

A multi-site, hospital-based survey was conducted in 11 major hospitals in Ghana from November 2015 to April 2016. They aimed to identify and evaluate available acute stroke services in Ghana and the extent to which these services align with global best practice. A pre-tested, structured questionnaire was used to gather data on available hospital-based acute stroke services in the study sites, using The World Stroke Organisation Global Stroke Services Guideline as a reference for global standards. Their study confirmed previous reports of limited and variable provision of evidence-based stroke services and the low priority for stroke care in resource poor settings. The authors recommended health policy initiatives to enhance uptake of evidence based acute stroke services in order to reduce stroke-related mortality and morbidity in countries such as Ghana. (Baatiema et al., 2017).

Baatiema and colleagues (2017) undertook a systematic search of the published literature to identify and compare evidence-based acute stroke management interventions with alternative care on overall patient mortality and morbidity outcomes, functional independence, and length

of hospital stay across Africa. Eligible studies were abstracted into evidence tables and their methodological quality appraised using the Joanna Briggs Institute checklist. Only four non-experimental studies (three cohort and one case series studies) were included in the final review. One study focused on the clinical efficacy of a stroke unit whilst the remaining three reported on thrombolytic therapy. The results demonstrated a reduction in patient deaths attributed to stroke unit care and thrombolytic therapy. However, the limited number of eligible studies and methodological limitations compromised definitive conclusions on the extent of and level of efficacy of evidence-based acute stroke care interventions across Africa. Evidence from this review confirms the widespread assertion of low applicability and uptake of evidence-based acute stroke care in low- and middle-income countries (LMICs). Despite the limited number of eligible studies, the overall positive patient outcomes following such interventions demonstrate the applicability and value of evidence-based acute stroke care interventions in Africa.

Urimubenshi and colleagues (2018) acknowledged the limited availability of stroke services in African countries. They aimed to describe the status of stroke care in Africa. They undertook a systematic search of the published literature to identify recent publications that described stroke care in any African country. They included 38 publications representing 14 of the 54 African countries. This review provides an overview of stroke care in Africa and highlights the paucity of available data. Poor awareness of stroke signs and symptoms, shortages of medical transportation, health care personnel, and stroke units, and the high cost of brain imaging, thrombolysis, and outpatient physiotherapy rehabilitation services were reported as major barriers to providing best-practice stroke care in Africa.

6. Barriers to hyper-acute stroke care

Regarding reperfusion therapy, several obstacles need to be overcome in order to reduce the symptom-to-needle time (arrival to emergency department (ED) to the administration of thrombolysis). Most time is lost in the pre-hospital period, the so-called “symptom-to-door time”, largely because many patients tend to wait before they seek medical attention. However, this is difficult to accomplish because campaigns aimed at raising public awareness of stroke symptoms have only limited impact on behaviour. (Van Wijngaarden, 2009) Within the hospital the focus should be on decreasing the time from arrival to intravenous thrombolysis (IVT) administration, the so-called “door-to needle time” (DNT). Besides improved functional outcome, a reduction in the DNT would increase the proportion of patients eligible for IVT

allowing more patients to be treated within the 4.5-hour time period from onset of symptoms (Kruyt, 2013).

As the benefits of IVT in acute ischemic stroke are time dependant, guidelines recommend an arrival to treatment initiation time or door to needle time (DNT) < 60 minutes. A multicentre study conducted in 1082 hospitals in the United States collected data of acute ischemic stroke patients treated with tPA within 3 hours of symptom onset between April 1, 2003, to September 30, 2009. Of the 25504 ischemic stroke patients that were treated with intravenous tPA, the DNT time was < 60 minutes in only 6790 (26.6%) (Fannorow et al., 2011). Patient factors most strongly associated with DNT of less than 60 minutes were younger age, male gender, white race, or no prior stroke. Hospital factors associated with less than 60-minute DNT included greater annual volumes of tPA-treated stroke patients. The proportion of patients with DNT of less than 60 minutes varied widely by hospital participating in this study (0% to 79.2%) and increased overall from 19.5% in 2003 to 29.1% in 2009. Symptomatic intracranial haemorrhage after treatment with tPA was less frequent for patients with door-to-needle times < 60 minutes compared with patients with door-to-needle times > 60 minutes (4.7% versus 5.6%). The authors concluded that less than one-third of the patients treated with intravenous tPA had a DNT of less than 60 minutes, with only modest improvement occurring over the 6.5 year period. They recommended a targeted initiative in order to improve the timelines of reperfusion treatment in acute ischemic stroke.

Meretoja and others analysed the effect of interventions aimed to reduce treatment delays in their single-center observational study in Finland. They included a total of 1,860 patients treated between June 1995 and June 2011, which also included 174 patients with basilar artery occlusion (BAO) treated mostly beyond 4.5 hours from symptom onset. In the non-BAO patients, there was a progressive reduction in the DNT annually, from a median of 105 minutes in 1998, to 60 minutes in 2003 and a further reduction to a mean of 20 minutes in 2011. They concluded that with multiple concurrent strategies it was possible to reduce the median in-hospital delay to 20 minutes. In order to achieve this objective, they proposed that much of the initial assessment could be done while the patient was being transported to hospital with less time spent in the emergency unit (EU) (Meretoja et al., 2012).

7. Benefits of stroke unit care

A stroke unit is a dedicated and geographically defined part of a hospital that takes care of stroke patients in both the acute and immediate post-acute phase. It has specialized staff with

a coordinated multidisciplinary expert approach to treatment and care. It comprises core disciplines: medical, nursing, physiotherapy, occupational therapy, speech and language therapy, and social work (Langhorne, 1998). An essential component of the stroke unit model of care is established pathways and management protocols for acute and post-acute management of stroke (including pre-hospital and emergency unit management of stroke) with careful attention to active management of physiological abnormalities to maintain homeostasis. Stroke care is coordinated by multi-disciplinary team (MDT) with regular scheduled ward rounds attended by the full MDT to discuss management strategy for each patient.

Patients treated in stroke units have been shown to have a better outcome than those treated in general wards. Meta-analyses of controlled trials indicate that treating patients in stroke units reduces mortality, institutionalization, and dependency. Treatment in a stroke unit compared with treatment in a routine clinical setting has been shown in studies to reduce mortality as well as reduce the likelihood of dependency after stroke and institutionalization. (Langhorne P 1993; Cochrane Database Syst Rev 2002; Stroke Unit Trialists' Collaboration 1997 and 2002; Seenan, 2007). Stroke unit care incorporates many elements working together, and it is difficult to identify any specific factor responsible for better outcome.

Very few studies have assessed the efficacy of stroke unit care in developing countries. A local study documented the outcome of patients admitted to the first multidisciplinary stroke unit opened at a secondary hospital in Cape Town, South Africa. Patient outcomes including in-hospital mortality, resource utilization (length of hospital stay, CT brain scans performed, and tertiary hospital referral). Access to inpatient rehabilitation were recorded for all patients admitted to the hospital for 3 months before initiating multi-disciplinary stroke care and for 3 months after implementing multidisciplinary stroke care. Despite the limitations of the study, the authors demonstrated that multidisciplinary stroke care could be successfully implemented in a resource-constrained secondary-level hospital with a significant reduction in inpatient mortality and an increase in referrals for inpatient rehabilitation suggesting an overall improvement in stroke care.(deVilliers., 2009) Resource utilization in terms of length of hospital stay increased by a mean of 2 days but the number of CT brain scans performed and referral to a tertiary hospital did not increase significantly in this study. Several other studies from low-income countries on five continents that compared care in a discrete stroke ward with conventional care in a general ward noted lower death rates in the stroke-unit group than in the control group. Despite using various methodological approaches, the difference was

statistically significant for many of these studies. These findings show that stroke units outside high-income areas can improve outcomes, at least in terms of survival (Langhorne, 2012).

Ideally all stroke patients should be treated in a stroke unit. A stroke unit was established in the year 2000 at Groote Schuur hospital (GSH) Western Cape, South Africa and offers a 24-hour service for evaluation and treatment of acute stroke cases including those suitable for reperfusion therapy with intravenous thrombolysis and more recently for endovascular mechanical thrombectomy.

All types of stroke patients, and not only those suitable for reperfusion therapy, benefit from treatment in a stroke unit. The sooner the patient is treated after symptom onset with measures to maintain homeostasis and prevent complications the better the likelihood for a good outcome which provides good cause to strive to reduce the barriers to acute care regardless of whether the stroke patient is a potential candidate for reperfusion therapy.

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PART B: Journal ready paper

Barriers to Acute Stroke Care at a Tertiary Hospital in the Western Cape, South Africa

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ABSTRACT

Background

Stroke guidelines recommend treatment of acute stroke as a medical emergency. In many countries prolonged delays occur before patients with acute stroke receive medical attention. Only a small percentage are assessed in hospital within the time window for reperfusion therapy. There is limited available published data concerning barriers to acute stroke care in South African patients.

Aims

To determine the pre-hospital barriers and in-hospital delays to emergency care for patients presenting to Groote Schuur Hospital (GSH) with acute stroke.

Methods

Study setting and design:

GSH is a tertiary academic level hospital in Cape Town, Western Cape province, South Africa. This study was a prospective, observational study with two components: a semi structured interviewer administered questionnaire and a record review of ischaemic stroke patients' clinical notes within 48 hours of admission to GSH.

Study-population:

Eligible patients were those with a clinical and radiological diagnosis of acute stroke who presented to GSH emergency unit and required admission for more than 24 hours. Recruitment took place over a 6-week period.

Results

Demographics: 50 patients were included, with a median age 61,5 (IQR 44,7 – 70,2) years; gender: females, 29 (58%). **Ethnicity:** Mixed African ancestry 38 (76%), Black 11 (22%).

Pre- hospital barriers: The median distance to hospital was 12,7 (IQR 10,2 – 17,6) km. Most patients 32 (64%) called for assistance immediately. In the 18 patients who delayed seeking assistance, the two most common reasons for the delays were: waiting for improvement 7 (38,9%), and failure of symptom recognition 4 (22%). Most of the patients 32 (64%) used their own private transport and half (25) of patients presented directly to GSH.

In- hospital delays: The median arrival at emergency unit to doctor assessment time interval for all the patients was 67,5 (IQR 19,75 – 128,5) minutes. Median door to CT brain time interval for all patients was 5,1 (IQR 1,7 – 10,2) hours and 3,1 (IQR 0,8 – 9,6) hours for those patients that arrived within thrombolysis window. Only 21 of 50 patients were referred to and assessed by the stroke unit. Only 3 of the 21 patients received intravenous thrombolysis and none received mechanical thrombectomy for the duration of the study.

Conclusion:

Most of the patients who arrived early at GSH used their own transport and lived close to hospital. Pre-hospital barriers were failure to recognize symptoms, patients hoping for improvement, delays in ambulance transport and routing via secondary hospitals. In hospital delays were prolonged door to doctor assessment and door to CT Brain time intervals.

KEY WORDS

CT	= Computed tomography
DNT	= Door to needle time
EMS	= Emergency medical service
EVT	= Endovascular thrombectomy
FAST	= Face, arm, speech, time
GSH	= Groote Schuur Hospital
HREC	= Human Research and Ethics Committee
IVT	= Intravenous thrombolysis
NNT	= Number needed to treat
MR	= Magnetic resonance
RCT	= Randomized controlled trials
SA	= South Africa

BACKGROUND

Stroke guidelines recommend treatment of acute stroke as a medical emergency. In many countries prolonged delays occur before patients with acute stroke receive medical attention. Consequently, only a small percentage are assessed in hospital within the time window for reperfusion therapy. There is limited available published data concerning barriers to acute stroke care in South African patients.

AIMS AND OBJECTIVES

The aim of the study was to determine both the pre-hospital barriers and the in-hospital delays to emergency care for patients presenting to Groote Schuur Hospital (GSH) with acute stroke. The overall objective of the study was to prospectively assess a group of patients that present to GSH Emergency Unit with clinical and radiological evidence of acute stroke (irrespective of whether or not they presented within the therapeutic window for the re-vascularization therapy) in order to identify and determine the factors that resulted in either early arrival or prolonged delays following the onset of stroke symptoms.

STUDY RATIONALE

Data from this study could provide valuable information relating to any pre-hospital and in-hospital barriers to the emergency care of patients presenting to GSH with acute stroke. Information from this study could be used to advise on methods of improving pathways to overcome these barriers.

METHODS

Study setting and design

Groote Schuur Hospital has a 6-bed stroke unit and offers a 24-hour stroke response service for evaluation and treatment of acute stroke cases including all those patients suitable for reperfusion therapy with intravenous thrombolysis and more recently for endovascular mechanical thrombectomy. The Stroke Service evaluates patients with the diagnosis of stroke in the Emergency Unit and consults on similar patients in the hospital inpatient service and admits stroke patients directly to the 6 bed Stroke Unit located within the neurology ward. The Stroke Service roster with the names and contact details of the registrars and consultants on stroke call is available in the Emergency Unit and through the Hospital telephone exchange. The initial evaluation is conducted by the Emergency Unit physicians who can refer any stroke

patient to the registrar on call from the stroke response team. Given the limited number of beds in the stroke unit, admissions tend to favour patients who have suffered stroke with a prior good baseline and are considered to have good rehabilitation potential, young patients with no clear cause for stroke, or older patients with no clear risk factors, and those stroke patients with management difficulties. All such patients with acute stroke admitted to the Stroke Unit are evaluated according to established pathways and follow a schedule of diagnostic and therapeutic steps. When the Stroke Unit is full, the Emergency Unit will refer the patient to the medical registrar on call for further management in the general medical wards. The stroke unit team can continue to review the patient in the medical ward if required but all stroke patients suitable for reperfusion therapy, those patients with acute posterior fossa infarcts or haemorrhage, and those presenting to the EU with recent TIA are required to be assessed and followed up by the stroke response team regardless of whether or not a bed is available in the stroke unit.

This study was a prospective observational study over a 6-week period with two components: a semi structured interviewer administered questionnaire and a record review of ischemic stroke patients' clinical notes within 48 hours of admission to hospital. The questionnaire was administered by face-to-face interviews by the investigator with each participant and/or their closest relatives presenting with acute stroke within 48 hours of arrival to the GSH emergency unit. The objectives of the questionnaire were to assess the pre-hospital barriers to acute stroke care and the variables of this assessment are listed in table 1.

Table 1

Assessment of pre-hospital barriers to care:
Demographic data (age, gender, ethnicity, employment status, marital status, living alone, level of education, distance to GSH)
Time and date of onset of symptoms of stroke
Time interval between symptom onset to calling for assistance for transfer to hospital
Reason for delay in calling for assistance
Mode of transport to hospital
Time interval from calling for assistance to vehicle arrival
Transit time to GSH
Direct or indirect route of transfer to GSH (ie. direct to GSH or indirect route via intermediate

Community Health Centre or level 2 hospital)
If indirect, transit time to intermediate hospital
Delay interval at level of the intermediate hospital
Time interval between symptom onset of acute stroke and arrival at GSH

After the interviews were completed, a review of the participants' clinical notes was undertaken by the first author within 48 hours of the patients' admission to hospital in order to assess any in-hospital barriers to care. The variables for this review are listed in table 2.

Table 2

Assessment of in-hospital barriers to care:
Time interval between patient arrival in the EU and initial assessment by triage-nurse
Time interval between onset of symptoms and initial doctor assessment
Triage grade
Time interval between onset of symptoms and stroke service assessment.
Time interval between patient arrival in the EU and CT Brain scan completed.
Door to needle time for intravenous thrombolysis (where applicable)
Door to needle time for endovascular revascularization (where applicable)
Onset of stroke to needle time

Study population:

Eligible patients for inclusion in this study were those with a clinical and radiological diagnosis of acute stroke who presented to the emergency unit and that required admission for more than 24 hours. Every attempt was made to assess patients sequentially within 24 hours of being admitted avoiding selection bias. Convenience sampling was used considering timeframe as the main factor in order to obtain our sample size from stroke patients visiting the GSH emergency unit. Recruitment took place over a 6-week period and a convenient sample of 50 patients was selected.

Exclusion Criteria

Patients for whom the time of onset of stroke could not be reliably determined (for example aphasic patients or those whose relatives are unable to provide onset time), and those patients

presenting with subarachnoid haemorrhage and other stroke mimics were excluded from the study.

Data collection:

All data was collected by the first author over a 6-week period between July 2017 to mid-August 2017. Patients admitted to the GSH Emergency Unit with the clinical and radiological diagnosis of acute stroke were invited to participate in a face to face interview. These interviews were conducted by the first author in English, Xhosa, or Afrikaans with a translator. Participants were interviewed in a comfortable secluded area in the emergency unit, medical ward, or stroke unit and only one interview was conducted for each participant. Responses from the questions were transcribed onto the questionnaire form during the interview. The responses from these questionnaires were used to determine the prehospital barriers to acute stroke care. After the face to face interview with each participant (or close relative if patient was aphasic) had been completed, an audit of each patient's medical record was undertaken by the first author within the first 48 hours of the patient's admission to assess the in-hospital delays to acute stroke care. Patients were initially identified using the nurses' patient admission record book and the investigator confirmed the diagnosis by review of the clinical records following admission to the emergency unit and by clinical assessment (the first author is a member of the stroke team which responds to stroke referrals from the emergency unit). All data from the hospital record and clinical assessment was recorded on a data capture sheet (refer appendix 1) and entered on a spreadsheet for analysis.

Data analysis:

The data from the questionnaire and from the medical record was analysed separately. The categorical data has been summarized using frequency tables and descriptive data, such as the reason for the delay in calling for assistance, has been categorized. For the numerical data the means, standard deviations, medians and interquartile ranges were used to summarize the data and the decision about which measures were used was determined by the distribution of the data. Analysis of the data was conducted using standard statistical software SPSS (<https://www.ibm.com/analytics/spss-statistics-software>).

Ethical considerations:

This study was reviewed and approved by the University of Cape Town's Human Research Ethics Committee (HREC REF: 879/2016). The study was a prospective, observational study and did not involve any active treatment or intervention. There were no potential health or

safety risks associated with the study. Informed consent was obtained from all participants and personal information remained confidential and confined to the data capture sheet that was stored in a secure place. No participant identifiers were present in the dissertation or any publications that may arise from this study. Computerized data bearing patient identifiers was password protected. Investigators stated no conflict of interest and no external source of funding was sought. The study adheres to the declaration of Helsinki 2000.

RESULTS

The demographic data: the median (IQR) age of the cohort was 61,5 (44,7 – 70,2) years, figure 1. Gender distribution showed more females, 29 (58%) than males, 21 (42%). There was a predominance of Mixed African ancestry patients 38 (76%), followed by Black patients 11 (22%), and 1 (2%) Indian patient. The majority of patients had secondary school education 33 (66%), followed by those with primary school education 15 (30%), and only a minority of patients 2 (4%) had tertiary level education. The majority of patients were un-employed, 37 (74%) at the time of their stroke.

Pre- hospital delays: The median (IQR) distance to hospital was 12,7 (10,2 – 17,6) km. The majority of patients indicated that they had called for assistance immediately 32 (64%) after symptom onset. For the 18 patients who delayed seeking medical attention immediately after symptom onset, 7 (38,9%) patients had hoped and were waiting for clinical improvement, 4 (22%) failed to recognise that their presenting symptoms were due to stroke, 6 (33,4%) were alone and aphasic and unable to communicate and summon help at onset of their symptoms, and 1 patient reported that she had concealed her symptoms as she did not wish to be a burden to her family. The majority of patients in this cohort used their own transport, 32 (64%) to get to hospital. Half (25) of patients presented directly to GSH and arrived earlier within a median (IQR) of 2,5 (1,75 – 4,55) hours of symptom onset compared to the indirect group that routed via a secondary hospital and presented within a median (IQR) of 24,1 (7,7 – 44,0) hours.

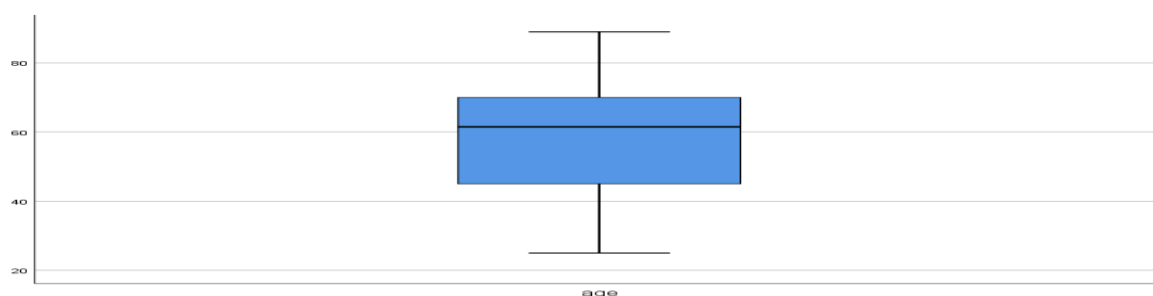


Figure 1: Box plot of age

In- hospital delays: All the stroke patients were triaged code orange irrespective of the time interval between symptom onset and their arrival at hospital. Triage grade orange requires urgent (but not immediate) management with a target of less than 10 minutes. The median (IQR) time interval from arrival at GSH (entrance security stamp) to assessment by the triage nurse was 6.0 (0-20,5) minutes. The median (IQR) time interval from arrival at GSH to the EU doctor assessment for all 50 patients was 67,5 (19,75– 128,5) minutes. The median (IQR) time interval from arrival to EU doctor assessment was 19 (5,5 – 81) minutes for the 23 patients that arrived within less than 4,5 hours of symptom onset. A CT brain scan was performed for all patients within a median (IQR) time interval of 5,1 (1,7 – 10,2) hours from arrival in the EU, but the 23 patients that arrived within less than 4,5 hours of symptom onset had an earlier CT brain scan within a median (IQR) time interval of 3,1 (0,8 – 9,6) hours after arrival in the EU. The 27 patients that arrived in more than 4,5 hours after symptom onset were scanned within a median (IQR) time interval of 5,3 (3,0 – 9,7) hours after arrival.

Of the 50 patients that were admitted to GSH with acute stroke, 21 (42%) were referred to the stroke service and were assessed by the stroke service within a median (IQR) time interval of 2,0 (1,4 – 10,2) hours after their arrival in the EU. Twelve of these patients arrived within less than 4,5 hours from symptom onset and were assessed by the stroke service within a median (IQR) time interval of 1,47 (0,8 – 1,8) hours of arrival in the EU. The remaining 9 patients that arrived more than 4,5 hours after symptom onset were assessed by the stroke service within a median (IQR) time interval of 11,9 (9,8 – 14,4) hours of arrival. These were typically non-urgent referrals to the stroke service requesting advice on further work-up or management or admission to the stroke unit when a bed became available. Only 3 of the 21 patients referred to the stroke response team received intravenous thrombolysis and none received mechanical thrombectomy.

DISCUSSION

The most consistently reported pre-hospital barrier in this study was the patient's or family's poor knowledge of stroke and stroke presentation which delayed their request for urgent medical help. This seems to be comparable with data from other developing countries. Surveys have shown that many people do not know the presenting symptoms of stroke (Weltermann et al., 2000). Several patients in this study had hoped and were waiting for clinical improvement after symptom onset or simply failed to recognise that their presenting symptoms were due to stroke whereas others were alone and aphasic at symptoms onset and unable to call for assistance. The majority of patients had no tertiary education, and most were unemployed at time of their stroke and lived in low-income areas including informal settlements which are some distance from the hospital. Most patients did, however, called for assistance immediately but due to ambulance delays, most patients used their own private transport to get to hospital. Half of patients presented directly to our hospital, but the remainder routed via a secondary hospital (without capacity to undertake any form of reperfusion therapy) with resultant delay in symptom onset to arrival time at our hospital. For the reasons cited above, most patients presented to our hospital outside the window of opportunity for reperfusion treatment.

The in-hospital delays that were identified included a delay in the time interval between arrival at the emergency unit (EU) and doctor assessment time which was more than an hour for all patients despite the code orange triage allocation. However, the median arrival time to EU doctor assessment time interval was 19 minutes for those patients that arrived within less than 4,5 hours of symptom onset. Notably, there was delay in the arrival to CT brain scan time interval of more than 5 hours for all patients. Those patients that arrived within the reperfusion therapy time window had an earlier CT brain scan done with a median time interval from arrival of just over 3 hours which is nevertheless excessively long given the time constraints critical to good outcomes with reperfusion therapies. Patients that present outside the reperfusion therapy window are not processed immediately. This study has also identified significant delays in door to CT Brain pathways likely caused by delays in nursing triage, delays in EU doctor assessment, delays in CT Brain booking, reliance on hospital porters to transfer patient to and from CT scanner, and hurdles in prioritizing stroke patients with other cases including trauma cases.

Only 21 (42%) of the 50 patients in this study were referred to the stroke service and they were assessed by the stroke service within a median time interval of 2,0 hours after their arrival in

the EU and those 12 patients that arrived within the therapeutic time window for reperfusion treatment were assessed by the stroke service within a median time interval of 1,47 hours of arrival in the EU leaving much scope for improvement in reaction times.

Limitations of this study were the relatively small sample size of 50 patients from a single centre and the limited recruitment time period of 6 weeks that is likely to have introduced a degree of selection bias. Although patients were recruited sequentially, some stroke patients that were referred from a secondary hospital for a CT brain scan were then immediately transferred back to these hospitals and were not included in the study. Acquisition of the data pertaining to the prehospital barriers to care relied on the patient or family member being able to give an accurate reliable account of the time of symptom onset and reasons for any delay in calling for assistance at the time of the onset of acute stroke symptoms. Clearly the pre and in-hospital delays and barriers to stroke care identified in this study at our institution are not necessarily a reflection of stroke care access and level of care available at other hospitals in the region.

In the Cape Town metropole there are 2 established stroke units at tertiary hospital with the necessary expertise and resources to offer reperfusion therapy for suitable patients with acute ischemic stroke. This prospective observational study has identified some of the important pre-hospital and in-hospital barriers that will need to be addressed and overcome if reperfusion therapy is to be delivered more effectively, efficiently and equitably at specialized stroke centres. According to our knowledge this is the first study that attempts to identify barriers to hyper-acute stroke care in South Africa at a state hospital where such resources are available.

The sooner the patient is treated after symptom onset with measures to maintain homeostasis and prevent complications the better the likelihood for a good outcome providing good cause to strive to reduce the barriers to acute care regardless of whether the stroke patient is a potential candidate for reperfusion therapy.

Regarding reperfusion therapy which is available at Groote Schuur Hospital for suitable patients with ischaemic stroke, the phrase “time is brain,” emphasizes that human nervous tissue is rapidly and irretrievably lost as stroke progresses and that therapeutic interventions should be emergently pursued (Gomez et al., 1993). The patient is estimated to lose approximately 1.9 million neurons each minute in untreated ischemic stroke (Saver et al., 2006). All guidelines emphasize rapid, safe and effective arterial recanalization to restore blood

flow through intravenous r-tPA and or endovascular therapy and improving functional outcome remains a primary objective of hyper-acute ischemic stroke management (Bryer et al., 2010). Treatment benefit is time-dependent and the sooner the treatment is given, the greater the chance of a successful outcome. The number needed to treat (NNT) to get one more favorable outcome drops from 4 within the first 90 minutes after symptom onset through to 7 at 3 hours, and towards 14 between 3 and 4.5 hours (Hacke et al., 2008).

Several obstacles need to be identified and overcome to reduce delays in treating patients with ischemic stroke. Much time is lost in the pre-hospital period in the so-called “symptom-to-door time”, largely because many patients tend to wait before they seek medical attention. However, this is difficult to accomplish because campaigns aimed at raising public awareness of stroke symptoms have only limited impact on behaviour (Van Wijngaarden, 2009). Within the hospital the focus should be on decreasing the time from arrival to commencement of treatment. Stroke patients who spend hours waiting to be assessed in the EU are more likely dehydrate or aspirate potentially resulting in poorer outcomes. For those who are suitable for reperfusion therapy, a reduction in the door-to needle time (DNT) or door to arterial puncture time could lead to improved functional outcome and an increase in the proportion of patients eligible for IVT allowing more patients to be treated within the 4.5hour time period from onset of symptoms (Kruyt, 2013).

Despite robust evidence of efficacy of reperfusion therapy for suitable patients with acute ischemic stroke we have encountered relatively few patients that present to GSH Emergency Unit early enough after symptom onset to potentially benefit from revascularization therapies such as intravenous thrombolysis and or endovascular therapy, and to receive early appropriate treatment to maintain physiologic homeostasis and prevent complications. As with many other low- and middle-income countries, the majority of patients in our setting experience prolonged delays between symptom onset and access to acute stroke care. Consequently, only a small proportion of stroke patients admitted to our hospital are potentially suitable candidates for revascularization therapy. If specific barriers to emergency care of stroke patients are identified and addressed, more patients could benefit from this type of treatment and measures directed at maintaining physiological homeostasis and preventing early complications could be implemented earlier.

Pre-hospital barriers to hyper-acute stroke care require attention as several studies have shown that public awareness programs reduce pre-hospital delays, but mass media campaigns, usually aimed at helping patients to identify the symptoms of stroke and the need to urgently call for help, are expensive and must be periodically repeated (Ringleb, 2008). The Heart and Stroke Foundation of South Africa has a crucial role to play in informing the broader South African public concerning recognition of symptoms of stroke and appropriate response to such symptoms. The Foundation actively promotes cardiovascular health through advocacy, influencing policy, providing information, tools, and support which will enable people to adopt healthy lifestyles and seek appropriate care early in the manifestations of the disease.

In many metropolitan areas, including Cape Town, the Emergency Medical Services (EMS) are under-resourced and over-burdened with volume and load of patients that they manage and transport. If more people are to benefit from acute stroke care, then it is essential to engage with the EMS to explore ways in which stroke patients can be identified more easily and promptly such as the use of FAST. FAST stroke is an algorithm used to help identify and enhance the response to a person having an acute stroke. (Goldstein et al., 2005) The acronym stands for Facial drooping, Arm weakness, Speech difficulties and Time of onset and to call emergency services. The FAST algorithm was developed in the UK in 1998 by a group of stroke physicians, ambulance personnel, and an emergency department physician and was designed to be an integral part of a training package for ambulance staff. FAST was created to expedite administration of reperfusion therapy. The EMS personnel could be enabled to identify stroke signs in a patient and the time of onset of symptoms and then determine whether the patient could feasibly be transported to one of the two tertiary hospitals in the metropole within a time window to allow for the option of reperfusion therapy. In such an instance the EMS could ideally give pre-hospital notification to the stroke centre of the pending arrival of such a patient and avoid routing via a secondary hospital. Pre-hospital notification could enable rapid alerting of the stroke response team while patient is still in transit to EU and significantly reduce the arrival to assessment time interval by the stroke service. For those patients arriving with private transport, the stroke response team should be notified of the presence of the stroke patient in the EU prior to the CT brain scan request so that a more rapid scan is facilitated by the stroke team as a means of reducing the arrival to CT brain scan time interval. In many stroke centres reperfusion with intravenous r-tPA takes place in the scanner by the stroke team. Other measures to overcome in-hospital barriers to stroke care include implementing pragmatic protocols and pathways with flow diagrams of acute stroke care for the emergency unit that

includes stroke triage. Simulation training is a means to identify delays and improve the efficiency of the emergency pathways and stroke protocol at a stroke centre. DNT was shortened in all 5 stroke centers participating in simulation studies in the Czech Republic. (Svobodova et al., 2018) Simulation training has been shown to be a powerful tool for improving hospital logistics. Ongoing training of stroke unit and emergency department medical and nursing staff in acute stroke care remains an essential component of any measures aimed at improving management.

More high-quality studies are needed to better understand barriers to acute stroke care in South Africa where resources are limited. This study has identified significant delays in both pre and in-hospital acute stroke management and highlights the need for improvement in stroke management pathways. This can be achieved by further training of the emergency services personnel (including staff managing the call-centres) on how to identify patients with acute stroke and those that are potential candidates for reperfusion treatment who can then be transferred directly to the appropriate hospital with a stroke service. The stroke team together with the emergency unit medical, triage, and nursing personnel at hospitals with a stroke service are also likely to benefit by regular stroke training including simulation training (such training is offered by the Angels Initiative in South Africa) in order to develop a more efficient acute stroke care pathway and standard operating procedure aimed at reducing treatment delays. Once such interventions have been implemented a further study would be of value to determine the efficacy of the intervention at the facility.

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Appendix 1 : Data collection sheet

PARAMETERS	PATIENT DETAILS	TIME IN MINUTES
1 ST name		
Surname		
Folder number		
Age		
Date of birth		
Gender		
Ethnicity		
Level of education		
Address		
Distance to hospital		
Employment Y/N		
Mobile 1		
Mobile 2		
Mobile 3		
Date of stroke		
Time of stroke		
Time interval to calling assistance for transfer to Hospital		
Reason for delay		
Mode of transport		

Time interval from calling assistance to vehicle arrival		
Transit time to GSH		
Direct or indirect to GSH		
name of intermediate hospital		
Symptom onset to arrival at intermediate hospital		
Symptom onset to arrival at GSH (door)		
Triage grade		
Arrival to assessment time - nurse		
Arrival to assessment time- doctor		
Onset to doctor assessment time		
Arrival to stroke service assessment time		
Symptom onset to stroke service assessment time		
CT Brain Y/N		
Date CT Brain		
Time of CT Brain		
Door to CT Brain time		
Door to needle time –ivi tPA		
Symptom onset to ivi tPA time		

Reason for not receiving thrombolysis		
Door to needle time -EVT		
Symptom onset to EVT time		